

Claims

1. A human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide which comprises the amino acid sequence of SEQ ID NO:2.

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2. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide of claim 1, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:4.

3. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide of claim 1, wherein
10 the polypeptide consists of the amino acid sequence of SEQ ID NO:4.

4. A human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide comprising a fragment or variant of the polypeptide of claim 1, wherein the fragment or variant comprises the amino acid sequence of SEQ ID NO:2.

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5. A human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule which encodes the polypeptide of any of claims 1-4.

6. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 5,
20 wherein the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

7. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 5,
25 wherein the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:3.

8. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 5,
wherein the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule consists of the nucleotide sequence of SEQ ID NO:3.

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9. The human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 8,
wherein the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid is a homolog or

allele of the nucleic acid sequence of SEQ ID NO:3.

10. A fragment of the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 5.

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11. An expression vector comprising the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 5 operably linked to a promoter.

12. An expression vector comprising the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid molecule of claim 10 operably linked to a promoter.

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13. A host cell transformed or transfected with the expression vector of claim 11.

14. An agent which selectively binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide of claim 1 or a nucleic acid that encodes the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide of claim 1.

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15. The agent of claim 14, wherein the agent is a polypeptide which binds selectively to the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide.

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16. The agent of claim 15, wherein the polypeptide is a monoclonal antibody or a polyclonal antibody.

17. The agent of claim 15, wherein the polypeptide is an antibody fragment selected from the group consisting of a Fab fragment, a $F(ab)_2$ fragment and a fragment including a CDR3 region.

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18. The agent of claim 14, wherein the agent is an antisense nucleic acid which selectively binds to a nucleic acid encoding the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide.

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19. The agent of claims 14-18, wherein the agent is an inhibitor of the calcium channel

activity of the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide.

20. A composition comprising a pharmaceutically acceptable carrier and a component selected from the group consisting of the polypeptide of claim 1, the nucleic acid molecule of claim 5 and the agent of claim 14.

21. A method for inhibiting human N-type calcium channel $\alpha_{1B+SFVG}$ subunit activity in a mammalian cell comprising

contacting the mammalian cell with an amount of a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit inhibitor effective to inhibit calcium influx in the mammalian cell.

22. The method of claim 21, wherein the inhibitor is selected from the group consisting of an antibody which selectively binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide, an antisense nucleic acid which binds a nucleic acid encoding human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide and a dominant negative human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide.

23. A method for treating a subject having a stroke, neuropathic pain, or traumatic brain injury comprising

administering to a subject in need of such treatment an inhibitor of the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide in an amount effective to inhibit voltage regulated calcium influx.

24. The method of claim 23, wherein the inhibitor is selected from the group consisting of an antibody which selectively binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide, an antisense nucleic acid which binds a nucleic acid encoding human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide and a dominant negative human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide.

25. The method of claim 23, wherein the inhibitor is administered prophylactically to a subject at risk of having a stroke.

26. A method for increasing human N-type calcium channel $\alpha_{1B+SFVG}$ subunit expression in a cell comprising

contacting the cell with a molecule selected from the group consisting of a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid and a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide, in an amount effective to increase voltage regulated calcium influx in the cell.

27. The method of claim 26, wherein the cell is contacted with one or more human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunits of the human N-type calcium channel or nucleic acids encoding such subunits.

28. A method for increasing calcium channel voltage regulated calcium influx in a subject comprising

administering to a subject in need of such treatment a molecule selected from the group consisting of a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit nucleic acid and a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide in an amount effective to increase voltage regulated calcium influx in the subject.

29. A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with increased or decreased voltage regulated calcium influx mediated by a human N-type calcium channel comprising

providing a cell or other membrane-encapsulated space comprising a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit polypeptide;

contacting the cell or other membrane-encapsulated space with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, cause a first amount of voltage regulated calcium influx into the cell or other membrane-encapsulated space;

determining a test amount of voltage regulated calcium influx as a measure of the effect of the lead compounds for a pharmacological agent on the voltage regulated calcium influx mediated by a human N-type calcium channel, wherein a the test amount of voltage regulated calcium influx which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces voltage regulated calcium

influx and wherein a test amount of voltage regulated calcium influx which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases voltage regulated calcium influx.

- 5 30. The method of claim 29, further comprising the step of loading the cell or other membrane-encapsulated space with a calcium-sensitive compound which is detectable in the presence of calcium, wherein the calcium-sensitive compound is detected as a measure of the voltage regulated calcium influx.
- 10 31. A method for identifying compounds which selectively bind a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform comprising,
providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform,
providing a second cell or membrane encapsulated space which expresses a human N-
15 type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the α_{1B} isoform expressed,
contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,
determining the binding of the compound to the first cell or membrane encapsulated
20 space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space but does not bind the second cell or membrane encapsulated space is a compound which selectively binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform.
- 25 32. A method for identifying compounds which selectively bind a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform comprising,
providing a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid,
providing a human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide
30 or nucleic acid,
contacting the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide

or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid, wherein a compound which binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid but does not bind the human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid is a compound which selectively binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform.

33. A method for identifying compounds which preferentially bind a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform comprising,

providing a first cell or membrane encapsulated space which expresses a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform,

providing a second cell or membrane encapsulated space which expresses a human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform, wherein the second cell or membrane encapsulated space is identical to the first cell except for the α_{1B} isoform expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound,

determining the binding of the compound to the first cell or membrane encapsulated space and the second cell or membrane encapsulated space, wherein a compound which binds the first cell or membrane encapsulated space in an amount greater than the compound binds the second cell or membrane encapsulated space is a compound which preferentially binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform.

34. A method for identifying compounds which preferentially bind a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform comprising,

providing a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid,

providing a human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid,

contacting the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid and the human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide

or nucleic acid with a compound,

determining the binding of the compound to the human N-type calcium channel

$\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid and the human N-type calcium channel

non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid, wherein a compound which binds

- 5 the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid in an amount greater than the human N-type calcium channel non- $\alpha_{1B+SFVG}$ subunit isoform polypeptide or nucleic acid is a compound which preferentially binds the human N-type calcium channel $\alpha_{1B+SFVG}$ subunit isoform.

- 10 35. A method for selectively treating subject having a condition characterized by aberrant brain neuronal calcium current comprising,

administering to a subject in need of such treatment a pharmacological agent which is selective for a human N-type calcium channel $\alpha_{1B+SFVG}$ subunit, in an amount effective to normalize the aberrant neuronal calcium current.

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